DOI:
10.1016/j.ajodo.2016.06.025

Document Version
Peer reviewed version

The effect of supplemental vibrational force on orthodontically-induced inflammatory root resorption - a multicenter randomized clinical trial

ABSTRACT

Introduction: A multicenter parallel three-arm randomized clinical trial was carried out in one university and two district hospitals in the UK to investigate the effect of supplemental vibrational force on orthodontically-induced inflammatory root resorption (OIIRR) during the alignment phase of fixed appliance therapy. **Methods:** Eighty-one subjects <20 years-old with mandibular incisor irregularity undergoing extraction-based fixed-appliance treatment were randomly allocated to supplementary (20-minutes/day) use of an intra-oral vibrational device (AcceleDent®) (n=29); an identical non-functional (sham) device (n=25) or fixed appliances only (n=27). OIIR was measured blindly from long cone periapical radiographs of the upper right central incisor taken at start of treatment (T1) and at the end of alignment (T3) when a 0.019 x 0.025-inch stainless steel archwire was placed (mean follow-up: 201.6 days; 95% CI: 188.6 to 214.6 days). Data were analyzed blindly on a per-protocol basis, since losses to follow-up were minimal, with descriptive statistics, one-way analysis of variance and univariable/multivariable regression modeling. **Results:** Nine patients were excluded from the analysis, which were evenly distributed across groups. Mean overall OIIRR measured amongst the 72 patients was 1.08 mm (95% CI: 0.89 to 1.27 mm). Multivariable regression indicated no significant difference in OIIRR for the AcceleDent (difference: 0.22 mm; 95% CI: -0.20 to 0.64; P=0.300) or AcceleDent-sham groups (difference: 0.26 mm; 95% CI: -0.28 to 0.80; P=0.339) compared to the fixed-appliance only group, after accounting for patient sex, age, alignment time (T1-T3), maximum pain experienced, history of dento-alveolar trauma and initial root length of the upper right central incisor. No other side-effects were recorded apart from pain and OIIRR. **Conclusions:** The use of supplemental vibrational force during the alignment phase of fixed appliance orthodontic treatment does not affect OIIRR associated with the maxillary central incisor tooth. **Registration**: ClinicalTrials.gov (NCT02314975). **Protocol**: The protocol was not published before trial commencement. **Funding**: Functional and sham AcceleDent units were donated by the manufacturer; there was no contribution into the conduct or writing of this study.

INTRODUCTION

Background

Orthodontic-induced inflammatory root resorption (OIIRR) is considered a common pathological side-effect of orthodontic treatment with fixed appliances and is the consequence of a multifactorial sterile inflammation within the periodontal ligament. The prevalence of OIIRR among orthodontic patients has been reported as 73%,[1] 90%[2] and 100%[3] in studies using plain film radiographs, cone beam computed tomography or histology, respectively. OIIRR most commonly affects the maxillary incisor, mandibular incisor and first permanent molar teeth[4,5] and is usually mild in nature, with only around 16% of orthodontic patients having clinically-relevant shortening of at least one tooth.[6-9]

The aetiology of OIIRR is believed to be multifactorial with many factors influencing outcome, including root morphology,[10] history of dentoalveolar trauma,[4] patient age[6] and the presence of any underlying systemic inflammatory condition, such as asthma or allergy.[11-13] Factors related to orthodontic treatment include the level and direction of force,[14-18] type of force[19,20] and contact of tooth roots with cortical bone.[7,21] However, the specific role relating to many of these factors is poorly understood and there is only good evidence that heavier orthodontic forces cause greater OIIRR than light forces[22] and that increased treatment time positively correlates to increased OIIRR.[23]

The increased risk of OIIRR in association with prolonged orthodontic tooth movement makes shorter treatment duration a worthwhile goal. The use of supplemental vibrational force has recently been advocated as a method of accelerating orthodontic tooth movement and reducing overall treatment time. Vibrational force has long been recognised as anabolic for bone, having been used to potentially increase bone mass in astronauts exposed to prolonged periods of micro-gravity and terrestrials susceptible to bone loss, such as post-menopausal women and those confined to wheelchairs or bed.[24-26] In animal models, vibrational force has been shown to promote bony remodelling at sutures[27,28] and speed up orthodontic tooth movement.[29,30] Based on these data, several devices have been developed that are now commercially available and designed to deliver vibrational force directly to the dentition. One of these, AcceleDent® is a hands-free removable portable appliance consisting of an activator unit and mouthpiece, which provides a vibrational frequency of 30 Hz and force of 0.2 N. The patient bites gently onto a vibrating thermoplastic wafer, which is in contact with the occlusal surface of both the maxillary

and mandibular dentitions. The patient uses the appliance for a recommended period of 20 minutes per day and it is claimed that this will result in an acceleration of tooth movement and an overall reduction in orthodontic treatment time.[31]

There is currently data from retrospective studies and two randomized clinical trials showing evidence of increased rates of tooth movement and reduced pain when using fixed appliances combined with supplemental vibrational force.[32-34] However, retrospective studies are known to be associated with bias and an exaggeration of treatment effects,[35] whilst both the existing randomized trials are at risk of bias.[36] Indeed, advertisement claims and the promising results of the early pilot studies have not been confirmed by subsequent well-designed randomized clinical trials that have shown no improvement in either tooth alignment rates or pain experience associated with supplemental vibrational force.[37-39] Importantly, no studies have so far reported on whether the use of supplemental vibrational force has any impact on levels of OIIRR experienced by patients undergoing orthodontic treatment with fixed appliances. The single existing trial to date on OIIRR is a small pilot split-mouth randomized trial with a total of 15 patients, which indicated that AcceleDent had no significant effect on the total volume of root resorption associated with the first premolar teeth within a four week period.[40] However, the follow-up associated with this small unpublished study was too short to provide any significant data.

Objectives

The aim of this randomized clinical trial report was to investigate OIIRR experienced during tooth alignment with fixed orthodontic appliances supplemented with vibrational force provided by the AcceleDent appliance. The null hypothesis was that supplemental vibrational force does not impact on levels of OIIRR during the alignment phase of orthodontic treatment with fixed appliances.

METHODS

Trial design and changes after trial commencement

This was a three-arm parallel randomized controlled trial comparing the effects of supplemental vibrational force on OIIRR in adolescent patients undergoing orthodontic treatment with premolar extractions and fixed appliances in three UK centers. Ethical approval was obtained from the United

Kingdom National Research Ethics Service (South East London REC 3: 11/LO/0056) and written informed consent was received from all parents, guardians and children. All methods were performed in accordance with the approved guidelines and regulations. The trial was registered at the European Clinical Trials Database (EudraCT) (2014-004211-37) on 29 September 2014 and ClinicalTrials.gov (NCT02314975) on 25 November 2014. No changes to the methodology occurred following trial commencement. The data is presented according to the CONSORT statement.[41]

Participants, eligibility criteria, and settings

Participants were recruited from patients referred to the Orthodontic Departments at King's College London Dental Institute (Guy's Hospital) UK; Royal Alexander Children's Hospital, Brighton, UK; and William Harvey Hospital, Ashford, UK between July 2011 and May 2014. The former is based in a dental school while the latter two are based in district general hospitals. All provide comprehensive orthodontic services and treatment. The inclusion criteria pertained to the assessment of the trial's primary outcome and were: (1) under 20 years of age at treatment start; (2) no medical contraindications, including regular medication; (3) in the permanent dentition; (4) mandibular arch incisor irregularity; (5) extraction of mandibular first premolars as part of the orthodontic treatment plan. Patients who fulfilled these criteria were invited to join and consented appropriately.

Interventions

Participants were randomly allocated to one of three treatment groups: (1) Pre-adjusted edgewise fixed-appliance treatment with adjunctive daily use of a functional AcceleDent (OrthoAccel® Technologies, Inc, Houston, Texas, USA) vibrational device (Accel-group); (2) Pre-adjusted edgewise fixed-appliance treatment with adjunctive use of a non-functional (sham) AcceleDent device (Accel-sham); and (3) Pre-adjusted edgewise fixed-appliance treatment alone (Fixed-only group). Subjects allocated to functional or sham devices were given direct verbal and written instruction on operation and usage, and instructed to use the device for 20 minutes per day as per manufactor guidance. They were also shown the electronic timer, and therefore made aware that their compliance was being monitored. The sham device was identical to the active device in all respects, except that it did not vibrate when switched on. The fixed

appliance used was standardized between groups (MBT prescription 0.022-inch pre-coated 3M Victory series, 3M Unitek, Monrovia, USA) as was the archwire sequence used for the alignment phase of treatment: 0.014-inch, 0.018-inch, 0.018 x 0.025-inch nickel titanium and 0.019 x 0.025-inch stainless steel archwires. The dental arches were bonded from the first molars and the archwires ligated fully with conventional elastomeric ligation. Following initial placement of the appliance patients were seen on an approximately eight week basis. Progression into the next archwire only occurred if the previous archwire had become passive and the new archwire could be fully ligated into the bracket slot. The archwires were cut distal to the first molars and were not cinched. No bite planes, auxiliary arches, inter-maxillary elastics, headgears or temporary anchorage devices were used during the period of investigation. All subjects were treated by ~~consultant~~ senior orthodontists (ATD, NJ, CS, JG); or experienced orthodontic residents ~~specialist registrars~~ (NRW, MA) under their direct supervision.

Outcomes

The main outcome for this report was the amount of OIIRR that occurred during the alignment phase of treatment using fixed orthodontic appliances, as measured from the maxillary right central incisor. This was planned as a secondary outcome of a randomized trial with the primary outcome of tooth alignment rate.[38] Specifically, OIIRR was measured from long cone periapical radiographs (LCPA) taken at the start of treatment (T1) and at the end of alignment on insertion of a 0.019 x 0.025-inch stainless steel arch wire (T3). Measurements were made directly from scanned radiographs using Adobe Photoshop CS3 Version 10 (Adobe Systems, Inc., San Jose, CA, USA) using the Ruler Tool to the nearest 0.1 mm by a single operator (ATD) who was blinded to which group the patient was in. The difference in root length from the LCPA taken at T1 and T3 was determined using a correction factor to account for differences in enlargement between the two films based on the measured crown length[4] (Fig. 1). There were no changes to outcomes following trial commencement.

An additional outcome was the number of patients with severe OIIRR, which was defined in this study as OIIRR greater than 2 mm measured from the LCPAs.[9]

Finally, data on maximum pain on a 100 mm visual analogue scale and analgesic use during the initial alignment phase were available from a previous trial report,[39] whilst the prevalence of any

dentoalveolar trauma on the maxillary incisors was assessed through patient history and clinical or radiographical examination. Both these factors were used as covariates in the analyses.

Sample size calculation

Sample size calculation for this trial was based upon the primary outcome of initial rate of orthodontic tooth alignment, which gave a required sample of 23 patients per group and has been described previously.[38] A previous investigation of OIIRR differences between two bracket systems adopted a difference of 0.4 mm as being clinically significant to calculate sample size.[42] A *post-hoc* power calculation after code breaking for the secondary outcome of OIIRR, using the above mentioned difference, a root mean squared error incorporating the variance of the OIIRR from the present trial and a 5% level of significance indicated that the present trial would have a power of 25-30%.

Randomization

The randomization sequence was generated by one investigator (MTC) using GraphPad online software (http://www.graphpad.com/quickcalcs/index.cfm) with unrestricted equal participant allocation (1:1:1) and undertaken centrally at King's College London, independently from the clinical operators, following recruitment (allocation concealment).[43]

Blinding

Whilst treating clinicians and subjects could not be blinded to the use of AcceleDent, subjects were not told if they were allocated to a functional or a sham appliance, which were identical in appearance, although the sham appliance did not vibrate ~~were initially blinded to the allocation of functional or sham appliances as they were identical in appearance with the exception that the sham appliance did not vibrate~~. The extracted data including the LCPAs were coded, so that both the outcome assessor (ATD) and statistician (SNP) were blinded to subject allocation. The coding of the data was broken after the end of the analysis and no breach of blinding was identified.

Statistical methods

Conventional descriptive statistics, including means and Standard Deviations (SDs) were used to present the demographic data for each group while differences between the groups were assessed using Analysis of Variance (ANOVA) for continuous data and chi-square for binary data, after checking for homoscedacity and normality of residuals. Regression modelling was carried out to assess the influence of the intervention on the two secondary outcomes of this trial, both individually using univariable modeling and collectively, using multivariable modeling. Generalized linear models and their extension to the binomial family were used, estimating Relative Risks (RRs) rather than odds ratios for the latter, due to their advantages. Multivariable analyses included all possible confounders, including initial root length, alignment duration, maximum pain reported from the patient during alignment[39] use of painkillers during alignment, and history of any kind of dentoalveolar trauma during the alignment phase.

Reproducibility of the measurements was determined by repeated measurement of 20 sets of radiographs made 2 weeks apart from the same outcome assessor (ATD) by calculating the Intraclass Correlation Coeffient (ICC), the average difference of the two readings, and the 95% Limits of Agreement (LA), according to the Bland-Altman method ~~and its 95% Confidence Interval (CI)~~. A 2-tailed P-value of 0.05 was considered statistically significant with a 95% Confidence Interval (CI) for all tests. All analyses were carried out prior to code-breaking using Stata 12.0 (Statacorp, College Station, TX, USA) by a single person (SNP) blinded to the allocation, except for the *post hoc* power calculation, which was conducted after code breaking.

RESULTS

Recruitment and participant flow

A total of 81 patients were recruited between July 2011 and May 2014 and randomized to the three experimental groups: 29 to the Accel-group, 25 to the Accel-sham group and 27 to the Fixed-only group. Participant flow through the trial is shown in the CONSORT flow diagram (Fig. 2). From the 81 randomized patients, a total of 9 were lost: 3 discontinued the intervention (one in each experimental group) and 6 had at least one radiograph that was unavailable (one, two and three patients in the Accel-group, Accel-sham and Fixed-only groups, respectively). Data for 72 patients was available for analysis at T3; missingness was classified as *missing-at-random,* as it was not dependent on baseline characteristics

or randomization. A complete case-analysis approach was used; by which, cases with missing outcome data were omitted from a particular analysis.

Baseline data

Distribution of subjects for trial site, randomization, baseline characteristics, and covariates is shown in Table I. The three groups were adequately balanced for all baseline characteristics. The mean duration of the study period (T1-T3) was 201.6 days (95% CI: 188.6 to 214.6 days) with no difference among groups.

Secondary outcome (OIIRR): calculation and precision

The OIIRR at T3 ranged from 0.00 mm to 3.60 mm with a mean of 1.08 mm (SD: 0.81; 95% CI: 0.89 to 2.7) for the whole sample. The measured OIIRR varied minimally amongst the three groups at T3 (Table II), with the Accel-group having a mean of 1.09 mm (SD: 0.64; 95% CI: 0.84 to 1.35), Accel-sham a mean of 1.16 mm (SD: 0.94; 95% CI: 0.75 to 1.58) and the Fixed-only group, a mean of 1.00 mm (SD: 0.9; 95% CI: 0.61 to 1.38) (P=0.794) (Fig 3). Multivariable regression indicated no significant difference in OIIRR for either the Accel-group (difference: 0.22 mm; 95% CI: -0.20 to 0.64; P=0.300) or the Accel-sham group (difference: 0.26 mm; 95% CI: -0.28 to 0.80; P=0.339) compared to the Fixed-only group after accounting for any confounders (Table III).

Secondary outcome (number of patients with severe OIIRR): calculation and precision

The number of subjects with severe OIIRR (greater than 2 mm) was 12 (17%) with no difference amongst groups (Table IV) (P=0.551). Multivariable regression indicated no significant difference in the proportion of subjects with severe OIIRR for the Accel-group (RR: 0.94; 95% CI: 0.13 to 7.09; P=0.955) or the Accel-sham group (RR: 1.35; 95% CI: 0.29 to 6.26; P=0.705) compared to the Fixed-only group, after controlling for confounding (Table V).

Reliability and agreement

The intra-rater reliability was excellent for all radiographic measurement, including crown length at T1 (ICC: 0.978; ~~95% CI: 0.946-0.991~~ average difference: -0.07; 95% LA: -0.43 to 0.30), root length at T1

(ICC: 0.998; ~~95% CI: 0.995-0.99~~ average difference: -0.01; 95% LA: -0.34 to 0.33), crown length at T3 (ICC: 0.976; ~~95% CI: 0.941-0.990~~ average difference: 0.02; 95% LA: -0.42 to 0.45) and root length at T3 (ICC: 0.997; ~~95% CI: 0.992-0.999~~ average difference: -0.05; 95% LA: -0.41 to 0.32).

Harms

Apart from orthodontic pain during initial alignment[39] and OIIRR, no other harms were found.

DISCUSSION

Main findings

According to the results of this trial, the null hypothesis could not be refuted, as the use of supplemental vibrational force during the alignment phase of fixed appliance treatment did not have a significant effect on OIIRR measured from LCPAs of the upper right central incisor. The levels of OIIRR in each group were similar and correspond to previous reports for orthodontic treatment using fixed appliances.[4-7,10,44] Additionally, OIIRR measured at the maxillary central incisor was not significantly influenced by age or sex of the patient, initial root length, history of dentoalveolar trauma during treatment, relative duration of the alignment phase or pain experience during this phase. Finally, the proportion of patients with severe OIIRR (>2 mm) was in agreement with previous studies[4,9,45], similar amongst experimental groups and therefore not influenced by the use of vibrational force.

This was a multicenter study with strict randomization and allocation concealment, partial blinding of clinician and patient, and full blinding of both outcome assessor and statistician. The three groups were comparable for sex, age and baseline malocclusion, making any differences found amongst groups more easily attributed to the administered intervention. Drop-outs were minimal, evenly distributed across the three groups, and irrespective of randomization; therefore, they should not have affected outcome. Finally, the distribution of patients in the three trial sites and their characteristics were similar, while the same treatment and measurement protocol was used in all of them.

The risk of severe OIIRR in this study according to the multivariable regression analysis decreased in the Accel-group by 6% and increased in the Accel-sham group by 35% compared to the Fixed-only group; both being statistically insignificant. However, the large imprecision (judged from the

large standard errors) combined with the minimal relative risks indicate that this finding is more likely to be a random artifact and therefore should be discarded.

As far as the outcome measurement was concerned, the ICCs showed very good reproducibility from the LCPAs. It has been reported that plain film radiographs can only detect OIIRR affecting the apex of the tooth, whilst OIIRR can occur on any part of the root surface. A more meaningful measure of OIIRR could have been obtained using a CBCT approach. However, this would expose the subjects to much higher doses of ionizing radiation and would have been unethical. Also, it is debatable whether OIIRR not detectable on a plain film radiograph would be of any clinical relevance, as comparable proportions of moderate or severe OIIRR have been shown with both CBCT and LCPAs.[46] It was therefore felt that the protocol of taking LCPAs reflected current clinical practice, making the trial results meaningful and applicable to a pragmatic context of routine orthodontic treatment in adolescents.

This component of the randomized controlled trial only investigated OIIRR during the alignment phase of treatment; however, the rate of alignment and duration of treatment was comparable to other similar studies.[47,48] It is possible that as treatment progresses, the use of vibratory force may influence levels of OIIRR experienced, particularly during the subsequent phase with a 0.019 x 0.025-inch stainless steel archwire. However, evidence of OIIRR early in treatment is correlated with final levels of OIIRR after treatment completion.[9,49,] Therefore, even though the study only followed the patients during the initial alignment phase, this should give an indication of whether the study intervention had an effect on overall levels of OIIRR.

This study specifically investigated OIIRR associated with the upper right central incisor tooth, as it has been previously reported that the maxillary incisors are amongst the teeth most commonly affected by OIIRR.[4,5] The upper right central incisor should therefore be representative of any generalized level of OIIRR experienced. Of course, it is possible that other teeth were affected to a greater or lesser extent, but to assess this would have required greater exposure of the patients to ionizing radiation, which was also considered ethically unacceptable.

The patients randomized to an active or sham device were all asked to use their respective AcceleDent units for 20 minutes per day and 20 minutes before each appointment. All units had a built-in timer that measured how many times the unit had been used each week. Unfortunately these timers

proved unreliable, were prone to breakage and only recorded whether the unit was turned on; not whether it was actually in the mouth when it was on. Therefore, whilst compliance data was collected it was incomplete and not included in the analysis, which is a potential limitation of this study. However, compliance was monitored verbally during the study and patients were asked to bring the appliances with them at each visit, when they were inspected for evidence of use. Encouragement was given at each visit and the majority of patients reported good compliance.

Limitations

A potential limitation of this study is the absence of definitive compliance data relating to use of the active and sham devices, which was problematic.[38] A lack of true blinding may also be regarded as a limitation, but complete blinding of operators and subjects was not feasible, whilst outcome measurement and statistical analyses were conducted blindly. Additionally, the effect of AcceleDent on root resorption could not be associated with the specific tooth movement of each tooth during alignment, but rather with the alignment phase as a whole. Finally, this part of the trial describing the secondary outcome of OIIRR was considerably underpowered (25-30% power), as the sample size calculation for the primary trial was based on rate of initial alignment, as previously reported.[38] ~~However, lack of power did not pose a considerable threat, as the largest~~ According to the OIIRR difference between groups ~~was minimal (0.16 mm) and it is highly improbable that this would have any clinical relevance~~ that was found in this trial, a sample size of over 200 patients would be needed to achieve enough power. However, such a large-scale trail might be difficult to justify, given the questionable clinical relevance of AcceleDent's effect on OIIRR (0.10 to 0.26 mm) and the fact that AcceleDent had not a significant effect on treatment efficiency.

Generalizability

This investigation was what we would consider a real-world study, carried out in a clinical environment typical of many where issues of compliance are encountered on a daily basis and the study was conducted during the initial stages of treatment, when compliance may be considered to be more forthcoming. We feel that despite the lack of reliable compliance data and reduced power, the results are still applicable to orthodontic practice in the wider setting and should be reported.

CONCLUSIONS

1. The use of supplemental vibrational force for 20 minutes per day does not have a significant impact on the level of OIIRR experienced by adolescent patients during the alignment phase of fixed appliance orthodontic treatment.
2. The proportion of patients having severe OIIRR (>2 mm) was not significantly influenced by the use of supplemental vibrational force.
3. Additional trials with adequate sample size are needed to adequately assess the possible impact of vibrational force on the observed OIRR during fixed appliance orthodontic treatment.

ACKNOWLEDGEMENTS

We are grateful to OrthoAccel Technologies Inc, who provided the functional and sham AcceleDent units. This investigation was undertaken independently from OrthoAccel Technologies Inc . The authors declare no potential conflicts of interest with respect to the authorship and/or publication of this research article.

Author contributions statement

ATD contributed to study design, data acquisition, data analysis and writing of the manuscript; NW, NJ, CS, JG and MA contributed to data acquisition and writing of the manuscript; SNP contributed to data analysis and interpretation, and writing of the manuscript; MTC contributed to study design, data analysis and interpretation, and writing of the manuscript. All authors reviewed the final manuscript, have given final approval and agree to be accountable for all aspects of the work.

Additional information

Competing financial interests

The authors declare no competing financial interests.

REFERENCES

1. Lupi JE, Handelman CS, Sadowsky C. Prevalence and severity of apical root resorption and alveolar bone loss in orthodontically treated adults. Am J Orthod Dentofacial Orthop 1996;109:28-37.
2. Lund H, Gröndahl K, Hansen K, Gröndahl HG. Apical root resorption during orthodontic treatment. A prospective study using cone beam CT. Angle Orthod 2012;82:480-7.
3. Brezinak N, Wasserstein A. Root resorption after orthodontic treatment: Part 1. Literature review. Am J Orthod Dentofacial Orthop 1993;103:62-66.
4. Linge L, Linge BO. Patient characteristics and treatment variables associated with apical root resorption during orthodontic treatment. Am J Orthod Dentofacial Orthop 1991;99:35-43.
5. Sameshima GT, Sinclair PM. Predicting and preventing root resorption: part 1. Diagnostic factors. Am J Orthod Dentofacial Orthop 2001;119:505-10.
6. Linge BO, Linge L. Apical root resoprtion in upper anterior teeth Eur J Orthod 1983;5:173-83.
7. Mirabella AD, Artun J. Prevalence and severity of apical root resorption of maxillary anterior teeth in adult orthodontic patients. Eur J Orthod 1995;17:93-9.
8. Sameshima GT, Sinclair PM. Characteristics of patients with severe root resorption. Orthod Craniofac Res 2004;7:108-114.
9. Artun J, Van 't Hullenaar R, Doppel D, Kuijpers-Jagtman AM. Identification of orthodontic patients at risk of severe apical root resorption. Am J Orthod Dentofacial Orthop 2009;135:448-55.
10. Smale I, Artun J, Behbehani F, Doppel D, van't Hof M, Kuijpers-Jagtman AM. Apical root resorption 6 months after the initiation of fixed orthodontic therapy. Am J Orthod Dentofacial Orthop 2005;128:57-67.
11. McNab S, Battistutta D, Taverne A, Symons AL. External apical root resorption of posterior teeth in asthmatics after orthodontic treatment. Am J Orthod Dentofacial Orthop 1999;116:545-551.
12. Owman-Moll P, Kurol J. Root resorption after orthodontic treatment in high- and low- risk patients: analysis of allergy as a possible redisposing factor. Eur J Orthod 2000;22:657-663.
13. Makedonas DT. Orthodontically induced root resorption: a clinical and radiographic survey [dissertation]. Gothenburg, Sweden: University of Gothenburg; 2012.

14. Harris DA, Jones AS, Darendelier MA. Physical properties of root cementum: part 8. Volumetric analysis of root resorption craters after application of controlled intrusive light and heavy orthodontic forces: a microcomputed tomography scan study. Am J Orthod Dentofacial Orthop 2006;130:639-47.
15. Chan E, Darendelier MA. Physical properties of root cementum; part 5. Volumetric analysis of root resorption craters after application of light and heavy orthodontic forces. Am J Orthod Dentofacial Orthop 2005;127:186-95.
16. Barbagallo LJ, Jones As, Petocz P, Darendelier MA. Physical properties of root cementum; part 10. Comparison of the effects of invisible removable thermoplastic appliances with light and heavy orthodontic forces on premolar cementum Am J Orthod Dentofacial Orthop 2008;133:218-27.
17. Paetyangkul A, Turk T, Elekdag-Turk S, Jones AS, Petocz P, Darendeliler MA. Physical properties of root cementum: part 14. The amount of root resorption after force application for 12 weekson maxillary and mandibular premolars: a microcomputered-tomography study. Am J Orthod Dentofacial Orthop 2009;136:492.e1-9.
18. Wu AT, Turk T, Colak C, Elekdag-Turk S, Jones AS, Petocz P, et al. Physical properties of root cementum: part 21. Root resorption after the application of light and heavy extrusive orthodontic forcesfor 4 weeks: a microcomputed tomography study. Am J Orthod Dentofacial Orthop 2011;139:e495-503.
19. Weiland F. Constant versus disipating forces in orthodontics: the effect on initial tooth movement and root resorption. Eur J Orthod 2003;25:335-42.
20. Aras B, Cheng LL, Turk T, Elekdag-Turk S, Jones AS, Darendelier MA. Physical properties of root cementum: part 23. Effects of 2 or 3 weekly reactivated continuous or intermittent orthodontic forces on root resorption and tooth movement; a micro-computes tomography study. Am J Orthod Dentofacial Orthop 2012;141:e29-37.
21. Kaley J, Phillips C. Factors related to root resorption in edgewise practice. Angle Orthod 1991;61:125-132.
22. Weltman B, Vig KWL, Fields HW, Shanker S, Kaizar EE. Root resoprtion associated with orthodontic tooth movement: a systematic review. Am J Orthod Dentofacial Orthop 2010;137:462-76.
23. Roscoe MG, Meira JBC, Cattaneo PM. Association of orthodontic force system and root resoprtion:

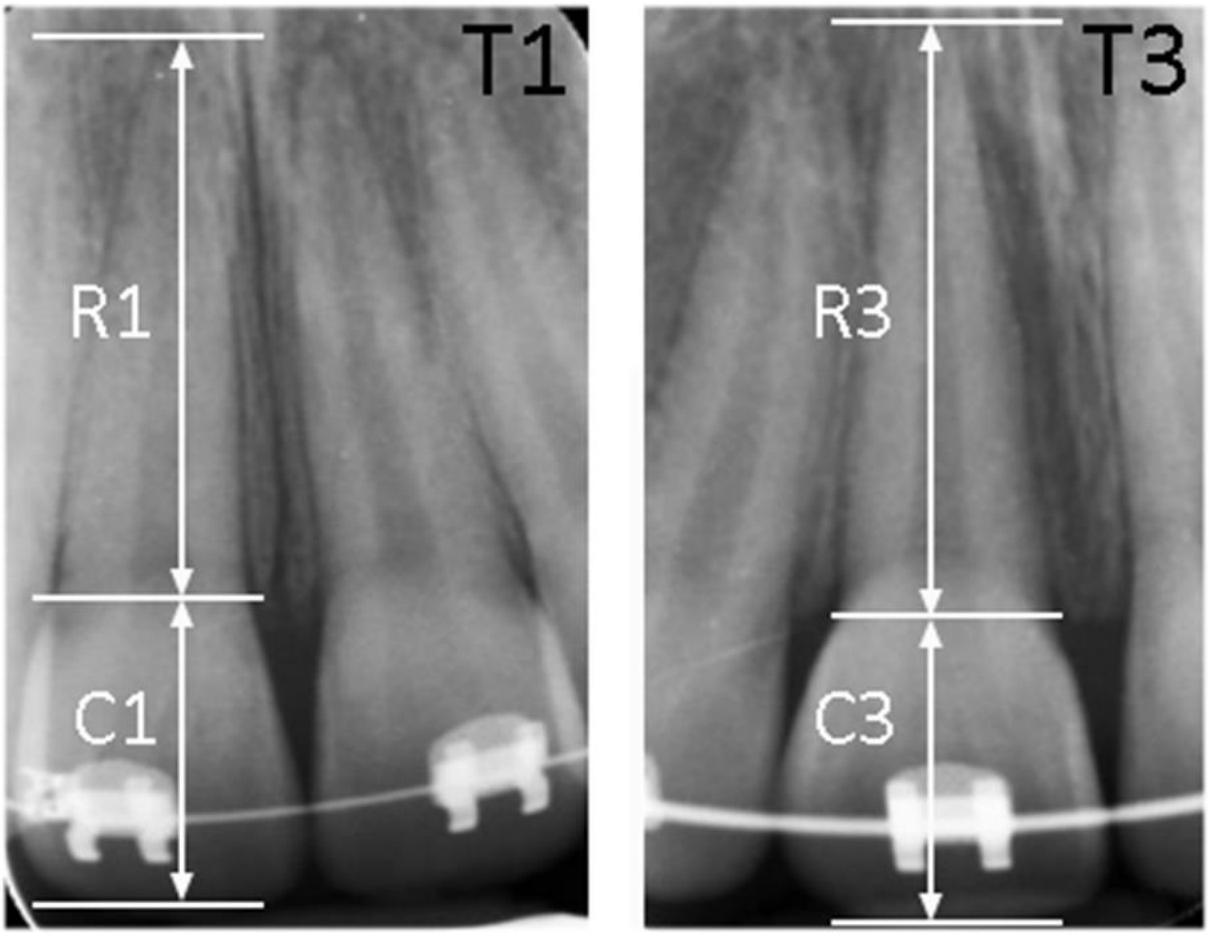
a systematic review. Am J Orthod Dentofacial Orthop 2015;147:610-26.

24. Rubin C, Recker R, Cullen D, Ryaby J, McCabe J, McLeod K. Prevention of postmenopausal bone loss by a low-magnitude, high-frequency mechanical stimuli: a clinical trial assessing compliance, efficacy, and safety. J Bone Miner Res 2004;19:343-351.
25. Ward K, Alsop C, Caulton J, Rubin C, Adams J, Mughal Z. Low magnitude mechanical loading is osteogenic in children with disabling conditions. J Bone Miner Res 2004;19:360-369.
26. Wang H, Wan Y, Tam KF, Ling S, Bai Y, Deng Y, et al. Resistive vibration exercise retards bone loss in weight-bearing skeletons during 60 days bed rest. Osteoporosis Int 2012;23:2169-2178.
27. Mao JJ, Wang X, Mooney MP, Kopher RA, Nudera JA. Strain induced osteogenesis of the craniofacial suture upon controlled delivery of low-frequency cyclic forces. Front Biosci 2003;8:a10-17.
28. Peptan AI, Lopez A, Kopher RA, Mao JJ. Responses of intramembranous bone and sutures upon in vivo cyclic tensile and compressive loading. Bone 2008;42:432-438.
29. Darendeliler MA, Zea A, Shen G, Zoellner H. Effects of pulsed electromagnetic field vibration on tooth movement induced by magnetic and mechanical forces: a preliminary study. Aust Dent J 2007;52:282-287.
30. Nishimura M, Chiba M, Ohashi T, Sato M, Shimizu Y, Igarashi K, et al. Periodontal tissue activation by vibration: intermittent stimulation by resonance vibration accelerates experimental tooth movement in rats. Am J Orthod Dentofacial Orthop 2008;133:572-583.
31. AcceleDent. Available at: http://www.acceledent.com/. Accessed on January 4, 2016.
32. Bowman SJ. The effect of vibration on the rate of leveling and alignment. J Clin Orthod 2014;48:678-688.
33. Pavlin D, Anthony R, Raj V, Gakunga PT. Cyclic loading (vibration) accelerates tooth movement in orthodontic patients: A double-blind, randomized controlled trial. Sem Orthod 2015;21:187-94.
34. Lobre WD, Callagari BJ, Gardner G, Marsh CM, Bush AC, Dunn WJ. Pain control in orthodontics using a micropulse vibraton device: a randomized clinical trial. Angle Orthod 2015 [Epub ahead of print].

35. Papageorgiou SN, Xavier GM, Cobourne MT. Basic study design influences the results of orthodontic clinical investigations. J Clin Epidemiol 2015;68:1512-22.
36. Savović J, Jones HE, Altman DG, Harris RJ, Jüni P, Pildal J, et al. Influence of reported study design characteristics on intervention effect estimates from randomized, controlled trials. Ann Intern Med 2012;157:429-38.
37. Miles P, Smith H, Weyant R, Rinchuse DJ. The effects of a vibrational appliance on tooth movement and patient discomfort: a prospective randomised clinical trial. Aust Orthod J 2012;28:213-218.
38. Woodhouse NR, DiBiase AT, Johnson N, Slipper C, Grant J, Alsaleh M, et al. Supplemental vibrational force during orthodontic alignment: a randomized trial. J Dent Res 2015;94:682-9.
39. Woodhouse NR, DiBiase AT, Papageorgiou SN, Johnson N, Slipper C, Grant J, et al. Supplemental vibrational force does not reduce pain experience during initial alignment with fixed orthodontic appliances: a multicenter randomized clinical trial. Sci Rep 2015 ;5:17224.
40. Tan 2011. The Effect of Mechanical Vibration (Acceledent, 30Hz) applied to the hemi-maxilla on Root Resorption Associated with Orthodontic Force. A Micro-CT Study [dissertation]. Sydney, Australia: University of Sydney; 2011.
41. Moher, D. Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. BMJ 2010;340: c869.
42. Leite V, Conti AC, Navarro R, Almeida M, Oltramari-Navarro P, Almeida R. Comparison of root resorption between self-ligating and conventional preadjusted brackets using cone beam computed tomography. Angle Orthod 2012;82:1078-82.
43. Schulz KF, Grimes DA. Allocation concealment in randomised trials: defending against deciphering. Lancet 2002;359:614-618.
44. Mohandesan H, Ravanmehr H, Valaei N. A radiographic analysis of external apical root resorption of maxillary incisors during active orthodontic treatment. Eur J Orthod 2007;29:134-9.
45. Marques LS, Ramos-Jorge ML, Rey AC, Armond MC, Ruellas AC. Severe root resorption in orthodontic patients treated with the edgewise method: prevalence and predictive factors. Am J Orthod Dentofacial Orthop 2010;137:384-8.

46. Ren H, Chen J, Deng F, Zheng L, Liu X, Dong Y. Comparison of cone-beam computed tomography and periapical radiography for detecting simulated apical root resorption. Angle Orthod 2013;83:189-195.
47. Scott P, DiBiase AT, Sherriff M, Cobourne MT. Alignment efficiency of Damon3 self-ligating and conventional orthodontic bracket systems: a randomized clinical trial. Am J Orthod Dentofacial Orthop 2008;134:470.e471-478.
48. Fleming PS, DiBiase AT, Sarri G, Lee RT. Efficiency of mandibular arch alignment with 2 preadjusted edgewise appliances. Am J Orthod Dentofacial Orthop 2009;135:597-602.
49. Levander E, Malmgren O. Evaluation of the risk of root resorption during orthodontic treatment: a study of upper incisors Eur J Orthod 1988;10:30-38.

FIGURES



$$OIIRR = R1\text{-}R3 \times C1/C3$$

TABLES

Table I. Baseline characteristics and covariates among the three groups

Baseline characteristic	Accel-group	Accel-sham	Fixed-only
Participants analyzed – n	27	22	23
Age (years) – mean (SD)	13.9 (1.6)	13.6 (1.6)	14.3 (1.9)
Age (range)	12.0-17.0	12.0-19.0	12.0-19.0
Male / female – n	14 / 13	11 / 11	11 / 12
Trial site – n (%)			
Ashford	13	9	7
Brighton	10	10	10
Guy's	4	3	6
Initial irregularity at T1– mean (SD)	8.4 (4.3)	8.1 (3.4)	8.5 (3.7)
Initial root length – mean (SD)	17.9 (2.5)	18.2 (2.9)	17.6 (2.6)

Covariate			
Maximum pain during alignment– mean (SD)	76.5 (19.6)	67.0 (24.7)	75.7 (22.6)
Use of painkillers during alignment – n (%)	20 (74%)	13 (59%)	18 (78%)
Dentoalveolar trauma history – n (%)	2 (7%)	6 (27%)	3 (13%)
Alignment time T1-T3 (days) – mean (SD)	210.4 (66.6)	207.2 (48.8)	186.1 (42.3)

SD, standard deviation.

Table II. Measured OIIRR across groups

	Accel-group	Accel-sham	Fixed-only	P*
n	27	22	23	
Mean (SD)	1.09 (0.64)	1.16 (0.94)	1.00 (0.90)	0.794
95% CI	0.84-1.35	0.75-1.58	0.61-1.38	

OIIRR, orthodontically induced inflammatory root resorption; *SD*, standard deviation; *CI*, confidence interval.

*Based on one-way ANOVA (root mean squared error=0.824; R-squared=0.007; P for heteroskedascity of residuals=0.134)

Table III. Univariable and multivariable regression of the mean measured OIRR

		Univariable model				Multivariable model			
		Coefficient	SE	95% CI	P	Coefficient	SE	95% CI	P
Experimental group	Accel-group	0.10	0.23	-0.36,0.56	0.678	0.22	0.21	-0.20,0.64	0.300
	Accel-sham	0.17	0.25	-0.32,0.65	0.499	0.26	0.28	-0.28,0.80	0.339
	Fixed-only	*Reference*				*Reference*			
Covariate	Patient sex					-0.11	0.19	-0.49,0.27	0.573
	Patient age					0.07	0.05	-0.03,0.17	0.145
	Maximum pain					0.00	0.00	-0.01,0.01	0.679
	Use of pain medication					0.05	0.19	-0.31,0.42	0.775
	Dentoalveolar trauma					0.13	0.36	-0.58,0.84	0.723
	Initial root length (T1)					0.04	0.04	-0.05,0.12	0.402
	Alignment time (T1-T3)					-0.00	0.00	-0.01,0.00	0.342

OIIRR, orthodontically induced inflammatory root resorption; *SE*, standard error; *CI*, confidence interval.

Table IV. Proportion of patients having OIIRR > 2mm

Overall		Accel-group		Accel-sham		Fixed-only		
n	Events (%)	*n*	Events (%)	*n*	Events (%)	*n*	Events (%)	P*
72	12 (17%)	27	3 (11%)	22	5 (23%)	23	4 (17%)	0.551

*based on chi-square test.

Table V. Univariable and multivariable regression of the number of patients having severe OIRR (> 2mm)

		Univariable model				Multivariable model			
		RR	SE	95% CI	P	RR	SE	95% CI	P
Experimental group	Accel-group	0.64	0.46	0.16,2.59	0.530	0.94	0.97	0.13,7.09	0.955
	Accel-sham	1.31	0.79	0.40,4.28	0.658	1.35	1.06	0.29,6.26	0.705
	Fixed-only	*Reference*				*Reference*			
Covariate	Patient sex					0.57	0.41	0.14,2.33	0.431
	Patient age					0.92	0.20	0.60,1.41	0.686
	Maximum pain					0.99	0.01	0.97,1.01	0.471
	Use of pain medication					1.98	1.76	0.35,11.28	0.440
	Dentoalveolar trauma					2.14	2.11	0.31,14.83	0.442
	Initial root length (T1)					0.91	0.23	0.56,1.48	0.703
	Alignment time (T1-T3)					1.00	0.01	0.98,1.01	0.665

OIIRR, orthodontically induced inflammatory root resorption; *RR*, relative risk; *SE*, standard error; *CI*, confidence interval.

FIGURE LEGENDS

Figure 1 Measurements from LCPAs of the maxillary right central incisor at T1 and T3, and calculation of OIIRR. Root length was measured as the distance between the apex of the tooth and the cementoenamel junction (R1 and R3); crown length was measured as the distance between the cementoenamel junction and the incisal edge (C1 and C3). A correction factor was calculated by dividing crown length at T1 (C1) by crown length at T3 (C3). Apical root resorption was measured as root length at T1 (R1) minus root length at T3 (R3), multiplied by the correction factor (C1/C3).

Figure 2 CONSORT diagram showing the flow of subjects through the trial.

Figure 3 Mean radiographic OIIRR in millimeters associated with the maxillary right central incisor after the alignment phase according to intervention (predictive margins with 95% CIs).